glibenclamide-induced cholestasis.[4] In view of the widespread use of glibenclamide, physicians should be aware of its hepatotoxic potential, even though glibenclamide-induced hepatotoxicity has been reported infrequently. The mechanism of this effect is not understood and is idiosyncratic, but, as exemplified by our patient, who had been on glibenclamide for several years, such hepatotoxicity may occur at any time during the course of therapy.

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REFERENCES

1. Carratu R, Parisi P, Frullone S. Glibenclamide-associated reversible cholestasis. Eur J Med 1992; 1:441–443

2. Del-Val A, Garrigues V, Ponce J, Benages R. Glibenclamide-induced cholestasis. J Hepatol 1991; 13:375

3. Goodman RC, Dean PJ, Redparvar A, Kitabchi AE. Glyburide-induced hepatitis. Ann Intern Med 1987; 106:837–839

4. Neuberger J. Drug-induced jaundice. Baillieres Clin Gastroenterol 1989; 3:447–466

Iliofemoral Venous Thrombosis Treated by Catheter-Directed Thrombolysis, Angioplasty, and Endoluminal Stenting

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ILIOFEMORAL DEEP VENOUS THROMBOSIS (DVT) accounts for over 20% of all DVTs.[1] Because of the extent of the thrombosis in iliofemoral DVT, traditional anticoagulant therapy with heparin sulfate is often inadequate to prevent both short- and long-term complications of DVT. Catheter-directed thrombolysis is a new technique for treating iliofemoral DVT; it overcomes many of the deficiencies of traditional therapy.[2,3] We report a case of a young woman with an extensive iliofemoral and inferior vena cava DVT treated successfully with catheter-directed thrombolysis. We also provide a review of this method of treating iliofemoral DVT.

(Fearon WF, Semba CP. Iliofemoral venous thrombosis treated by catheter-directed thrombolysis, angioplasty, and endoluminal stenting. West J Med 1998; 168:277–279)

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Report of a Case

An active 27-year-old woman presented two weeks after a 100-mile bike ride with low back pain, left thigh pain, and a 2-day-old fever. Her medications included an oral contraceptive pill and ibuprofen. The remainder of her history was unremarkable. On admission she had a temperature of 38.3°C (100.9°F). Her left inguinal area was extremely tender to the touch; there was trace edema at the ankle; and a pelvic examination showed a left adnexal mass. Laboratory studies were notable for a leukocyte count of 14.0×10^9 per liter (14,000 mm^3). Results of a pelvic ultrasound examination were normal; however, an abdominal CT scan revealed an extensive venous thrombosis extending from the bifurcation of the inferior vena cava through the left iliac venous system at least to the level of the common femoral vein. An ultrasound study of the left leg showed an occlusive deep venous thrombosis extending from the left external iliac vein to the left distal superficial femoral vein.

The patient was initially treated with intravenous heparin. Because her symptoms persisted, she underwent catheter-directed thrombolysis with urokinase on the hospital day 3. A venogram was performed (Figure 1A) and urokinase was infused via a catheter placed directly within the thrombus. The venography showed a high-grade stenosis with residual thrombus in a segment of the common iliac vein 48 hours into the infusion (Figure 1B). Angioplasty was performed, and an endoluminal stent was deployed. The result was improved flow (Figure 1C). The patient received urokinase for a total of 72 hours, and, after complete resolution of her pain and swelling and full mobility of her leg, she was discharged on hospital day 7 on oral anticoagulation. A hypercoagulable work-up was unremarkable except for a slightly low level of antithrombin III (80%), possibly secondary to the acute DVT and/or oral contraceptive use.

Our impression was that the patient had developed her DVT secondary to compression of her left iliac vein by her right iliac artery (May-Thurner or Cockett syndrome), perhaps enhanced while bicycle riding and exacerbated by low antithrombin III levels.[4,5]

Discussion

Standard therapy for iliofemoral DVT consisting of anticoagulation with heparin is often slow to relieve lower extremity pain and swelling and does not consistently prevent pulmonary embolism or the postphlebitic syndrome.[6–8] Surgical venous thrombectomy can rapidly restore blood flow, but it is hampered by rethrombosis and the postphlebitic syndrome as well.[9,10] Success with systemic thrombolytic treatment has been limited because an adequate amount of thrombolytic medication cannot be delivered to the more extensive clot without dramatically increasing hemorrhagic complications.[7]

Numerous studies of catheter-directed thrombolysis suggest that it can achieve venous thrombolysis rapidly, safely, and efficaciously.[2,3,7,11–13] Catheter-directed thrombolysis involves accessing the venous system via

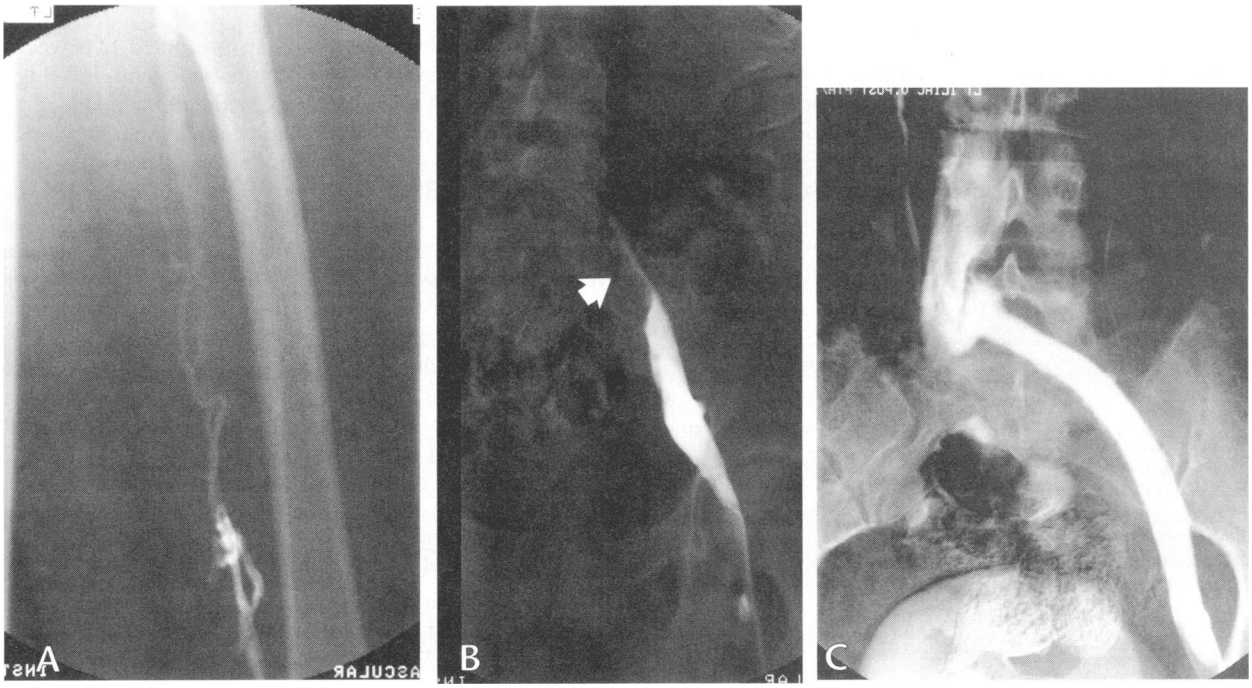

Figure 1.—These images are from a 27-year-old woman with acute left leg iliofemoral deep vein thrombosis. (A) Ascending venography demonstrates occlusion of the femoral vein secondary to deep venous thrombus and opacification of only a small tortuous venous collateral. After catheter-directed thrombolysis using urokinase, repeat venography (B) shows fully restored patency of the femoral vein and external iliac vein; however, there is persistent occlusion of the common iliac vein secondary to chronic organized thrombus (arrow). After angioplasty and endoluminal stenting venography, there is free-flow of contrast through the reconstructed segment of the iliac vein (C). The patient remained asymptomatic without recurrent DVT at 6-months follow-up.

the popliteal vein, inserting a guide wire across the thrombosed segment, and advancing a catheter into the thrombus. Urokinase is then delivered directly to the thrombus. In patients with more chronic or extensive thrombosis—in which venous damage has resulted in narrowing or stenosis—balloon angioplasty followed by placement of a stainless steel endoluminal stent can be performed to improve and maintain patency. The procedure can be performed in all patients with an acute iliac DVT, with or without involvement of the inferior vena cava, and femoral, popliteal, or calf veins; it cannot be performed, however, in those who have an absolute contraindication to anticoagulation therapy. The patients who have been found to respond best include those with a DVT of less than 4 weeks' duration. Patients who have had a DVT for more than 4 weeks are considered for the procedure if the thrombus involves only the iliac system and if there is normal inflow from the femoral venous system.[2]

Semba and Dake have reported their experience with catheter-directed thrombolysis in 32 patients (and 41 limbs).[2] Technical success, defined as less than 30% residual stenosis, was achieved in 85% of treated limbs. Clinical success, defined as complete or partial resolution of lower extremity pain and edema, was also achieved in 85% of treated limbs (complete resolution occurred in 80%). Complications were minimal; there were no deaths and no patients with oxygen desaturation or increased dyspnea to suggest pulmonary embolism. Because pulmonary embolism was not found to be a clinically detectable complication during early experiences, the authors of the study did not use baseline ventilation-perfusion scans or prophylactic inferior vena cava filters, although others have.[7] They hypothesize that the thrombotic fragments that theoretically break off and travel to the pulmonary arterioles are not clinically important—the fragments have urokinase bound to them and are lysed before they can result in pulmonary infarction.[3] In the follow-up period, which ranged from 0 to 45 months, symptoms had not recurred in any of the successfully treated patients.

Follow-up ultrasound evaluation in patients that were treated with a stent revealed a primary patency rate of 95%. Numerous smaller case series demonstrate similar results.[7,11–13] To date, however, no double-blind, randomized, prospective long-term studies have been done to compare the efficacy or cost of catheter-directed thrombolysis with traditional anticoagulation therapy. Nor have such studies been performed to determine the impact of catheter-directed thrombolysis on the incidence of delayed complications of iliofemoral DVT, such as the postphlebitic syndrome or recurrent DVT. Work in these directions may help solidify the role of catheter-directed thrombolysis in the treatment of iliofemoral DVT.

REFERENCES

1. Havig O. Deep vein thrombosis and pulmonary embolism: an autopsy study with multiple regression analysis of possible risk factors. Acta Chir Scand 1977; 478(Suppl 1):1–120

2. Semba CP, Dake MD. Catheter-directed thrombolysis for iliofemoral venous thrombosis. Sem Vasc Surg 1996; 9:26–33

3. Semba CP, Kee ST, Dake MD. Endovascular thrombolysis therapy for deep venous thrombosis. Sem Resp Crit Care Med 1996; 17:87–94

4. Ferris EJ, Lim WN, Smith PL, Casali, R. May-Thurner Syndrome. Radiology 1983; 147:29–31

5. Cockett FB, Thomas ML. The iliac compression syndrome. Brit J Surg 1965; 52:816–821

6. Strandness DE Jr, Langlois YE, Cramer M, Randlett A, Thiele BL. Long-term sequelae of acute venous thrombosis. JAMA 1983; 250:1289–1292

7. Tarry WC, Makhoul RG, Tisnado J, Posner MP, Sobel M, Lee HM. Catheter-directed thrombolysis following vena cava filtration for severe deep venous thrombosis. Ann Vasc Surg 1994; 8:583–590

8. Akesson H, Brudin L, Dahlstrom JA, Eklof B, Ohlin P, Plate G. Venous function assessed during a five-year period after acute iliofemoral venous thrombosis treated with anticoagulation. Eur J Vasc Surg 1990; 4:43–48

9. Lord RSA, Chem FC, Devine TJ, Benn IV. Surgical treatment of acute deep venous thrombosis. World J Surg 1990; 14:694–702

10. Plate G, Einarsson E, Ohlin P, Jensen R, Quarfordt P, Eklof B. Thrombectomy with temporary arteriovenous fistula: the treatment of choice in acute iliofemoral venous thrombosis. J Vasc Surg 1984; 1:867–876

11. Comerota AJ, Aldridge SC, Cohen G, Ball DS, Plisken M, White JV. A strategy of aggressive regional therapy for acute iliofemoral venous thrombosis with contemporary venous thrombectomy or catheter-directed thrombolysis. J Vasc Surg 1994; 20:244–254

12. Okrent D, Messersmith R, Buckman J. Transcatheter fibrinolytic therapy and angioplasty for left iliofemoral venous thrombosis. J Vasc Intervent Radiol 1991; 2:195–197

13. Molina JE, Hunter D, Yedlicka JW. Thrombolytic therapy for iliofemoral venous thrombosis. Vasc Surg 1992; 26:630–637